Conformational Effects in Cyclic Olefins. Kinetics and Stereochemistry of Epoxidation of Some Alkyl-Substituted Cyclohexenes[1]

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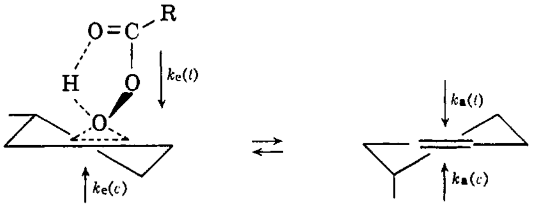
The rates of epoxidation of a number of substituted cyclohexenes suggest that the effects of remote alkyl groups are primarily steric rather than inductive in nature. Epoxidations of *cis*-4,5-dimethylcyclohexene and 3,3-dimethylcyclohexene occur at rates approximately half that of cyclohexene itself, implying strong retardation by the axial methyl. The stereoselectivity demonstrated in the *cis*-4,5-dimethyl system (87% *trans* epoxidation) supports the premise that this effect is steric in origin. The intermediate reaction rate and preferred formation of *trans* epoxide allow an approximate calculation of the conformational preference in 4-methylcyclohexene; it is suggested that the equatorial form is favored by approximately 1 kcal./mole.

Unlike the saturated analog cyclohexane, very little is known about conformational effects in substituted cyclohexenes. The paucity of data in this area stems largely from the difficulties associated with applying the usual methods of conformational analysis[2] to unsaturated materials. With regard to the cyclohexene ring itself Beckett, Freeman, and Pitzer[3] have suggested that the boat form is less stable than the half-chair (values of 2.2 and 2.7 kcal./mole were calculated). In the present work no compelling evidence for consideration of the boat form as an appreciable contributor to the conformational equilibria has been found.

More recently Sakashita,[4] using Raman and infrared spectroscopic methods, has concluded that the halogen in 4-bromocyclohexene is essentially devoid of conformational preference, while in 3-chloro- and 3-bromocyclohexene the axial conformation is preferred by 0.64 and 0.70 kcal./mole, respectively. Axial preference has also been established by Garbisch[5] for a number of 6-substituents in 1-phenylcyclohexene. The gross difference which may account for the relatively greater axial preference of 3- than 4-substituents appears to originate from the approach to eclipsed conformation of the 6- or 3-equatorial group with the adjacent vinyl substituent.

We chose to use a combined stereochemical and kinetic approach to the problem of conformational effects in alkyl-substituted cyclohexenes. In particular, epoxidation by peracid was chosen for reasons of convenience of rate determinations, and the anticipated ease of product analysis, either by direct v.p.c. measurement or by conversion to known derivatives. Winstein and Holness[6] and Curtin[7] have both stressed the general inadvisability of inferring ground-state conformational populations from product distributions, the latter being solely a property of differences in transition-state energies for kinetically controlled processes. However, we believe that epoxidation is one of a class of reactions which may be treated in a special manner, *i.e.*, in which the conformational effects in the ground state are transmitted quantitatively to the transition state. The product of this reaction in the case of cyclohexene oxide is known to exist with the six-membered ring in a half-chair form quite comparable to the olefin itself.[8] Unlike other reactions leading to cyclohexane derivatives, in which the transition state may lie conformationally between a half-chair and chair, the similarity in ground state and product for epoxidation strongly suggests that the transition state for this reaction will closely resemble the half-chair.

The spirano-form transition state for peracid epoxidation appears to be generally accepted.[9] There are then four conformationally distinct transition states to consider for a substituted cyclohexene, one of which is depicted and the others are implied by the symbols for the rate constants. The effect of a nonpolar group in the 4-position can now be examined; when this group exists in the equatorial conformation, it is far removed from the site of reaction and no effect on rate is expected. Similarly the rate constant for *trans* attack $[k_a(t)]$ when the alkyl group is axial should be unaffected by this group.[10] *cis* attack, on the other hand, would be diminished in this conformation by the interaction of the attacking peracid with the axial substituent. On the basis of the assumption $k_e(t) = k_e(c) = k_a(t) > k_a(c)$ one may predict that the over-all rate for the substituted cyclohexene will be lower than cyclohexene itself, and further that *trans* epoxide will be formed in greater amount than the corresponding *cis* isomer. In effect, application of both kinetic and stereochemical data will serve as a cross-checking device with regard to the assumptions in this argument.



Inductive effects may play an important role in epoxidation. Vinyl alkyl substituents are known to enhance the rate of reaction by large factors.[11] Hen-

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(1) Support by the Petroleum Research Fund, administered by the American Chemical Society, is gratefully acknowledged.

(2) H. H. Lau, *Angew. Chem.*, **73**, 423 (1961).

(3) C. W. Beckett, N. K. Freeman, and K. S. Pitzer, *J. Am. Chem. Soc.*, **70**, 4227 (1948).

(4) K. Sakashita, *Nippon Kagaku Zasshi*, **79**, 329 (1958); **80**, 13 (1959); **80**, 972 (1959); **81**, 49 (1960); *Chem. Abstr.*, **52**, 10721*c* (1958); **53**, 6762*h* (1959); **54**, 2008*h*, 12015*b* (1960).

(5) E. W. Garbisch, Jr., *J. Org. Chem.*, **27**, 4243, 4249 (1962).

(6) S. Winstein and N. J. Holness, *J. Am. Chem. Soc.*, **77**, 5562 (1955).

(7) D. Y. Curtin, *Record Chem. Progr.* (Kresge-Hooker Sci. Lib.), **15**, 111 (1954).

(8) B. Ottar, *Acta Chem. Scand.*, **1**, 283 (1947).

(9) E. S. Gould, "Mechanism and Structure in Organic Chemistry," Holt, Rinehart, and Winston, New York, N. Y., 1959, p. 534.

(10) More precisely, the absolute energy of this transition state will be higher than that for either $k_e(t)$ or $k_e(c)$ by an amount equal to the conformational preference of the alkyl substituent; however, this same interaction is present in the ground state and the effects will kinetically cancel.

(11) D. Swern, *J. Am. Chem. Soc.*, **69**, 1692 (1947); B. M. Lynch and K. H. Pausacker, *J. Chem. Soc.*, 1525 (1955).

best[12] has demonstrated that polar substituents exert a stereoselective influence on epoxidation and that in certain cases these effects are observable over long distances. The rates of addition of 2,4-dinitrobenzenesulfenyl chloride to various cyclohexene derivatives have been determined by Kwart and Miller,[13] and a reasonably linear plot of log K vs. σ_I has been obtained. The very similar relative rate sequences in this work and in the present epoxidation study suggest strongly that the transition states for both reactions have similar steric and electronic demands. While the data of Kwart and Miller support the proposal that inductive effects of polar substituents are rate controlling, a similar conclusion for remote alkyl substituents is not justified. It should be noted that the rates are depressed by alkyl substitution, opposite to the expected effect,[14a] requiring a redefinition of the inductive substituent constants for these nonpolar groups.[13] These new values, of questionable validity, have been used in subsequent work by Kwart and Takeshita.[14b] The present work indicates that the effects of 4-alkyl substituents are very nearly or entirely steric and conformational in nature. Inductive effects may be observable for 3-alkyl substituents but, while our data are not conclusive, they suggest a more important role for steric effects.

This view is supported by the absence of any positional effect on the rates of solvolysis of conformationally equivalent 3- and 4-*t*-butylcyclohexyl tosylates[6] (a reaction in which a good deal of positive charge is generated in the transition state), as well as by Henbest's observation that change of solvent did not affect the *trans–cis* ratio (76:24) in epoxidation of 4-methylcyclopentene.[12]

The kinetic data for epoxidation of a number of substituted cyclohexenes are shown in Table I. Some general conclusions are evident. All of the alkyl-substituted materials react slower than cyclohexene itself, as expected on the basis of steric and conformational arguments but not on the basis of inductive effects, which predict the opposite rate sequence. Of particular interest are *cis*-4,5-dimethylcyclohexene and 3,3-dimethylcyclohexene, both of which react approximately half as fast as cyclohexene. This is the expected value if an axial methyl group strongly retards attack by peracid.

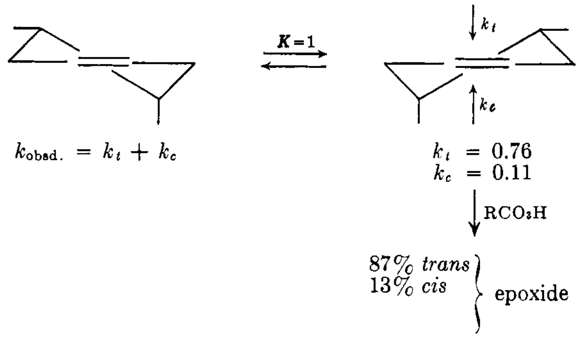
TABLE I

RATES OF EPOXIDATION OF SUBSTITUTED CYCLOHEXENES WITH *m*-CHLOROPERBENZOIC ACID IN ETHER AT 25°

Cyclohexene	10^3k, l. mole.$^{-1}$ sec.$^{-1\,a}$	Relative rates
Unsubstituted	1.88	100
4-*t*-Butyl	1.76	94
3-Methyl	1.77	94
4-Methyl	1.52	81
trans-4,5-Dimethyl	1.49	79
cis-4,5-Dimethyl	0.87	46
3,3-Dimethyl	0.83	44
cis-4,5-(–CH_2OCH_2–)	0.94	50
trans-4,5-(–CH_2OCH_2–)	0.55	29

[a] These values represent the average of from three to six determinations. The estimated average deviation is ±5% for a single determination; the rate constants were reproducible ±3% among various determinations.

This retardation should lead to a preponderance of *trans* epoxide in the reaction of *cis*-4,5-dimethylcyclohexene, and this is indeed observed.

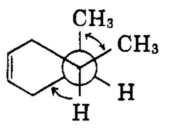


$k_\text{obsd.} = k_t + k_c$

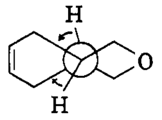
$k_t = 0.76$
$k_c = 0.11$

87% *trans*
13% *cis*
epoxide

This stereochemical result bears out the suggestion that the axial methyl group is specifically rate depressing. However, k_t is also 19% lower than the predicted value, 0.94×10^{-3} l. mole^{-1} sec.$^{-1}$ (half the value for cyclohexene). A plausible explanation for the rate diminution may lie in the flexibility of the cyclohexene ring. Expansion of the skew-dimethyl dihedral angle by rotation about the C-4–C-5 bond will force the remote axial hydrogen toward the reaction site (for *trans* attack), as illustrated by Newman projection.



In this connection the rates of epoxidation of *cis*- and *trans*-2-oxa-3a,4,7,7a-tetrahydroindan (last two entries in Table I) are of interest. The *cis* material has approximately the same over-all rate constant as *cis*-4,5-dimethylcyclohexene,[15] while the *trans*-oxatetrahydroindan reacts considerably slower. The approximate coplanarity of the five-membered ring may explain the diminished rate of this system, again due to torsional effects forcing the C-4 and C-5 hydrogens into the reaction plane.



The added complication of an apparently easily distorted half-chair is apparent in other systems as well. For instance, 4-*t*-butylcyclohexene is epoxidized 6% slower than cyclohexene, which on the basis of our kinetic model would indicate some contribution of *axial* conformation. However, the stereochemical evidence (Table II) contradicts this premise; the observed preferred formation of *cis* epoxide is not allowed by the simple model, which predicts a minimum of 50% *trans* material for a conformationally frozen system. We believe the stereochemical distribution is due to dis-

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(12) H. B. Henbest, *Proc. Chem. Soc.*, 159 (1963).

(13) H. Kwart and L. J. Miller, *J. Am. Chem. Soc.*, **83**, 4552 (1961).

(14) (a) For a recent discussion of inductive substituent constants, see M. Charton, *J. Org. Chem.*, **29**, 1222 (1964); (b) H. Kwart and T. Takeshita, *J. Am. Chem. Soc.*, **84**, 2833 (1962).

(15) This agreement may be fortuitous, depending on the magnitude of the inductive effect of the ether function and any specific directive influences associated with this group. The stereochemistry of this epoxidation is currently under investigation.

TABLE II

STEREOCHEMISTRY OF EPOXIDATION OF SUBSTITUTED CYCLOHEXENES WITH *m*-CHLOROPERBENZOIC ACID IN ETHER AT 25°

Cyclohexene	% *trans* epoxide
4-*t*-Butyl	39.5
4-Methyl	53.6
cis-4,5-Dimethyl	87

tortion of the half-chair by the bulky *t*-butyl group, which strongly prefers the equatorial orientation. On this basis the over-all rate constant may be dissected by the stereochemical factor, giving $k_c = 1.06$ and $k_t = 0.69$ ($\times 10^{-3}$). This distortion thus acts to increase the rate of *cis* attack and decrease the rate of *trans* attack relative to cyclohexene ($^1/_2k = 0.94$), behavior not unexpected on the basis of this explanation.[16]

It is clear that the simple model postulated for the epoxidation reaction may lead to contradictory kinetic and stereochemical results in other systems. Of particular interest is the question of conformational preference in 4-methylcyclohexene, and rather than abandon this model, it seems worthwhile to examine in detail the anticipated effects of methyl substitution due to ring distortion. 4-Methylcyclohexene does follow the original postulate in that the rate is depressed relative to cyclohexene and the *trans* epoxide is the predominant product. The *cis*-4,5-dimethylcyclohexene system gave evidence that prediction of an individual rate constant neglecting distortion of the ring by alkyl substitution would be erroneous. An approximation which allows calculation of the conformational preference in 4-methylcyclohexene is that the rate depression of the axial methyl group is proportional to the stereochemical effect observed in *cis*-4,5-dimethylcyclohexene, such that $k_e(t) = k_e(c) = k_a(t) = k_a(c)/n$, where $n = 13/87 = 0.16$. Calculations of the stereochemistry of epoxidation expected for various mole fractions of equatorial methyl conformation are shown in Table III. Inherent in the system is the relative insensitivity of stereochemical outcome to conformational preference, *i.e.*, a variation of only 13% in *trans* epoxide with a change from no preference to very strong equatorial preference. However, our evidence indicates the stereochemical results (Table II) are reliable to better than ±1%; setting these extreme limits gives an equilibrium consisting of 85 ± 5% equatorial methyl conformation, corresponding to a ΔF of 1.0 ± 0.2 kcal./mole. The calculation in Table III is also relatively insensitive to the value of n; *i.e.*, using 0.1 and 0.2 gives predicted *trans* epoxide values of 53.6 and 53.2% for 85% equatorial methyl olefin. In other words, some error in the initial approximation of rate ratios $k_e(t):k_a(c)$ is tolerable and does not strongly influence the calculation of conformational preference. On less certain ground is the assumption that $k_e(t) = k_e(c) = k_a(t)$, and because of this we must view the calculated conformational preference value as being of the proper order of magnitude rather than quantitatively precise.[17]

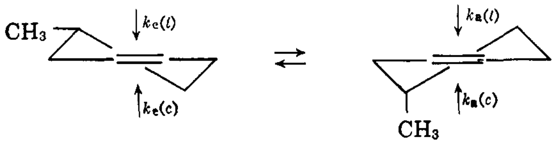
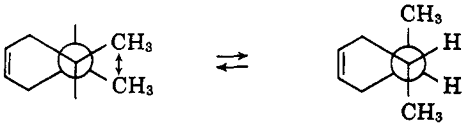


TABLE III

EXPECTED STEREOCHEMISTRY OF EPOXIDATION OF 4-METHYLCYCLOHEXENE

% equiv. methyl	% *trans* epoxide
50	63.3
75	56.0
80	54.7
85	53.5
90	52.3
100	50

The diequatorial conformation of *trans*-4,5-dimethylcyclohexene contains an added skew-butane interaction relative to equatorial 4-methylcyclohexene. This interaction would be expected to exert a torsional effect on the C-4–C-5 bond such that rate of epoxidation might be equal to or greater than that of cyclohexene. The observed depressed rate indicates that the diaxial conformation makes an appreciable contribution. This is predicted on the basis of the value for conformational preference of the alkyl group obtained from 4-methylcyclohexene, *i.e.*, (2 × 1.0) − 0.9 (skew-butane interaction) = 1.1 kcal./mole as the energy term favoring the diequatorial form.[18]



Purely on the basis of the kinetic data in Table I, by comparison of the rates of the unsubstituted olefin, 3-methyl-, and 3,3-dimethylcyclohexene, it would appear that the 3-alkyl group has a stronger preference for equatorial orientation than does the 4-analog. This is opposite to the effect found by Sakashita[4] in the halogen-substituted olefins, and further evidence is clearly required before any definite conclusions may be reached. We are currently determining the stereochemistry of epoxidation of 3-methylcyclohexene (which will require isomerically pure epoxide) and preparing other systems to amplify the evidence presented in this paper.

Experimental

Cyclohexene, 3-methylcyclohexene,[19] 4-*t*-butylcyclohexene,[20] and *cis*-2-oxa-3a,4,7,7a-tetrahydroindan[21] were prepared and purified by previously described procedures. Commercial 4-methylcyclohexene was found to contain trace impurities which could not be removed by distillation. A pure sample was ob-

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[16] Alternatively, the boat form with *t*-butyl group assuming the quasi-equatorial orientation could explain the preference for *cis* attack, using as analogy the strong preference of norbornene to form *exo* epoxide. However, it is not apparent from models that the presence of a bulky alkyl substituent should depress the energy of the boat form relative to the half-chair sufficiently to cause it to contribute appreciably as a transition state conformation, which would be required by the kinetic and stereochemical evidence presented.

[17] Added confidence in this value stems from comparison of methylcyclohexane, where the conformational preference (1.8 kcal./mole) stems largely from the 1,3-diaxial methyl-hydrogen interactions, to 4-methylcyclohexene, where to a first approximation only one such interaction is evident, suggesting a value about half as great.

[18] The nearly equal rates of epoxidation of *trans*-4,5-dimethylcyclohexene and 4-methylcyclohexene provide added evidence that steric and conformational effects rather than inductive effects are rate controlling.

[19] A. Berlande, *Bull. soc. chim. France*, **9**, 642 (1942). We wish to thank Stanley Wood for this preparation.

[20] J. Sicher, F. Sipos, and M. Tichy, *Collection Czech. Chem. Commun.*, **26**, 847 (1961).

[21] E. L. Eliel and C. Pillar, *J. Am. Chem. Soc.*, **77**, 3600 (1955).

tained from *p*-cresol (purified as the *p*-nitrobenzoate[22]), using the general procedure described for the 4-*t*-butyl analog.[20] The 4-methylcyclohexane that was obtained in this manner had b.p. 102–103°.[23]

3,3-Dimethylcyclohexene.—Commercial 2-methylcyclohexanol was oxidized by aqueous chromic acid in acetone to 2-methylcyclohexanone, b.p. 163–164°. Methylation of this material was accomplished using the procedure of Vanderwerf and Lemmerman.[24] Attempts to obtain pure 2,2-dimethylcyclohexanone by distillation of this mixture were only partially successful. A fraction containing mainly the desired material was collected at 168–171°. Lithium aluminum hydride reduction of this fraction gave a mixture of alcohols which was distilled through a 18-cm. spinning-band column at atmospheric pressure. The fraction which boiled at 176–177° was shown by vapor phase chromatographic analysis to contain about 95% 2,2-dimethylcyclohexanol.

The tosylate of this alcohol (18.5 g.) was prepared by treatment with 42 g. of *p*-toluenesulfonyl chloride in pyridine for 48 hr. at 0°. The ether extract was washed with water, 5% hydrochloric acid, and dilute bicarbonate, and then dried. Evaporation gave a solid which was recrystallized from pentane to give 23.8 g. (57%) of colorless crystalline material, m.p. 53–54°. This material was added to a solution (or slurry) of 15 g. of potassium *t*-butoxide in 200 ml. of collidine, and the resulting mixture was slowly brought to reflux. After 3-hr. reflux, the mixture was cooled and the olefinic product was isolated by normal procedures. The 3,3-dimethylcyclohexene (4.0 g., 43%) obtained in this manner boiled at 114–114.5° and showed a single peak on vapor phase chromatography; the n.m.r. spectrum contained a sharp singlet methyl peak, indicating no rearrangement on elimination.

Anal. Calcd. for C_8H_{14}: C, 87.2; H, 12.8. Found: C, 86.9; H, 12.6.

***cis*-4,5-Dimethylcyclohexene.**—An ice-cold solution of methanesulfonyl chloride (0.86 mole) in 450 ml. of anhydrous pyridine was added gradually to a cold solution of 60 g. (0.42 mole) of *cis*-4,5-di(hydroxymethyl)cyclohexene in 170 ml. of solvent. After standing 2 days at 0°, the mixture was treated with excess dilute hydrochloric acid solution and extracted twice with chloroform. After washing with bicarbonate solution and water, the chloroform extract was dried and evaporated. Recrystallization of the residue from methanol gave 53.6 g. (43%) of colorless crystalline dimesylate, m.p. 82.5–83°.

This product was reduced with 12.9 g. (0.34 mole) of lithium aluminum hydride in tetrahydrofuran; after refluxing 48 hr., isolation in pentane followed by distillation gave 9.9 g. (50%) of *cis*-4,5-dimethylcyclohexene, b.p. 123–124°.[13]

***trans*-2-Oxa-3a,4,7,7a-tetrahydroindan.**—Using the method employed for the *cis* compound,[21] 17.5 g. (0.125 mole) of *trans*-4,5-di(hydroxymethyl)cyclohexene[25] in 50 ml. of dry pyridine was treated with 23.8 g. of *p*-toluenesulfonyl chloride to give 10.5 g. (68%) of product, b.p. 77–78° at 18 mm.

Anal. Calcd. for $C_8H_{12}O$: C, 77.4; H, 9.7. Found: C, 77.0; H, 10.0.

***trans*-4,5-Dimethylcyclohexene.**—The ditosylate of *trans*-4,5-di(hydroxymethyl)cyclohexene was prepared in 60% yield by the method of Ayres and Raphael,[25] m.p. 93–94° (lit.[25] m.p. 94–95°). The reduction of this ditosylate (53.2 g.) in ether with 12.9 g. of lithium aluminum hydride produced 7.0 g. (54%) of *trans*-4,5-dimethylcyclohexene, b.p. 120–120.5°.

Anal. Calcd. for C_8H_{14}: C, 87.2; H, 12.8. Found: C, 87.0; H, 12.9.

Geometry of Epoxides of *cis*-4,5-Dimethylcyclohexene.—The products from several kinetic determinations with *cis*-4,5-dimethylcyclohexene were collected, washed free of excess *m*-chloroperbenzoic acid and *m*-chlorobenzoic acid, and evaporated to give a residue of epoxide. This crude material did not contain ketonic or hydroxylic products, as demonstrated by infrared and vapor phase chromatography, and was used directly in later experiments.

A sample was subjected to hydride reduction and the tosylate was prepared from this alcohol product. No purification steps were used to avoid isomeric fractionation. The crude tosylate was subsequently reduced with lithium aluminum hydride to give a mixture of olefins and saturated material; this mixture contained *cis*-1,2-dimethylcyclohexane but was free of the *trans* isomer, thus demonstrating that the geometry of the alkyl groups had remained intact during the syntheses. This was subsequently confirmed by comparing retention times of the *cis*- and *trans*-4,5-dimethylcyclohexenes on a dibutyl tetrachlorophthalate v.p.c. column.

Vapor phase chromatographic analysis of the epoxide from kinetic runs showed two peaks with areas of 87 ± 1 (*trans*) and 13 ± 1% (*cis*).

Lithium aluminum hydride reduction of this mixture gave two alcohols (analyzed as the acetates on a triscyanoethyoxypropane column) in a ratio of 77.5 (*trans*) and 22.5% (*cis*). Mixed hydride reduction gave, in agreement with our previously reported results for 4-*t*-butylcyclohexene,[26] 85.5% *trans* alcohol and 14.5% *cis*.

Rhodium on alumina reduction of 3,4-xylenol leads to a mixture of alcohols in which *cis*-dimethyl material predominates (97.6%), as shown by oxidation to ketones and subsequent analysis. The *cis*-dimethyl material consisted of 55% *cis* and 45% *trans* alcohol.

Equilibration of the product from mixed hydride reduction was accomplished by refluxing a mixture of 0.5 g. of alcohol, 0.5 g. of aluminum isopropoxide, 0.1 ml. of acetone, and 10 ml. of anhydrous isopropyl alcohol. Aliquots (1 ml.) were removed after 13, 36, 60, 80, and 96 hr.; the desired alcohols were isolated, and the acetates were prepared and analyzed. The last three samples did not vary, indicating that equilibrium had been attained. The final mixtures contained 52.3% *cis* and 47.7% *trans* alcohol. Simple theory, using typical *A* values for the ring substituents, predicts that the *trans* alcohol will be slightly favored (~57%); we do not presently have data to ascertain the reasons for this reversal in conformational preference, although it is presumably associated with a "buttressing effect" of the type discussed by Noyce and Dolby.[27]

The best evidence for structure of the alcohols and epoxides in this system was attained by lithium aluminum hydride reduction of *cis*-3,4-dimethylcyclohexanone. It is expected that the 3-methyl group will dictate the course of this reduction, because of its potential direct steric interaction with the reaction site. The 4-methyl group, on the other hand, is too remote for such interaction. Using as models 3,3,5-trimethylcyclohexanone and 3-methylcyclohexanone, which give 55[28] and 87%[29] *cis* alcohols, respectively, it is predicted that *cis*-3,4-dimethylcyclohexanone will give mainly *cis* alcohol; in fact, 86% *cis*- and 14% *trans*-3,4-*cis*-dimethylcyclohexanol is formed. The similarity of these results with those from 3-methylcyclohexanone suggests that the major transition state contributor is the 3e,4a-dimethyl conformation.

Epoxides of 4-*t*-Butylcyclohexene.—The detailed analysis of this mixture has been previously reported.[26]

Epoxides of 4-Methylcyclohexene.—We found no evidence of separation of the geometrical isomers in this system with any of a large number of vapor phase chromatography columns.

Reduction with lithium aluminum hydride gave a mixture of alcohols which was readily separable into axial (89.5%) and equatorial (10.5%) components by analysis on a diethylene glycol succinate (DEGS) column. We were unable to effect complete separation of the four isomeric products. The axial–equatorial ratio is very similar to that observed[26] with product obtained in this manner from 4-*t*-butylcyclohexene, and indicates that the methyl group is exerting a strong conformational effect in this reduction.

Mixed hydride reduction of the epoxide mixture gave 98% axial and 2% equatorial alcohols.

Both products were oxidized by the Jones chromic acid in acetone procedure; the resultant ketones were analyzed on the DEGS column; identical mixtures of 3- and 4-methylcyclohexanone were obtained on both cases. Area measurements were corrected (small, 0.5% correction) by comparison with known mixtures of the two ketones. The products contained 53.6 ± 0.2% 3-methylcyclohexanone and 46.4 ± 0.2% 4-methylcyclohexanone. These figures correspond to the amounts of *trans* and *cis* epoxide,

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[22] E. Hanggi, *Helv. Chim. Acta*, **4**, 23 (1921).

[23] H. Adkins and A. K. Roebuck, *J. Am. Chem. Soc.*, **70**, 4041 (1948).

[24] C. A. Vanderwerf and L. W. Lemmerman, "Organic Syntheses," Coll. Vol. III, John Wiley and Sons, Inc., New York, N. Y., 1955, p. 44.

[25] D. C. Ayres and R. A. Raphael, *J. Chem. Soc.*, 1788 (1958).

[26] B. Rickborn and J. Quartucci, *J. Org. Chem.*, **29**, 3185 (1964).

[27] D. S. Noyce and L. J. Dolby, *ibid.*, **26**, 3619 (1961).

[28] H. Haubenstock and E. L. Eliel, *J. Am. Chem. Soc.*, **84**, 2363 (1962).

[29] E. L. Eliel, *Record Chem. Progr.* (Kresge-Hooker Sci. Lib.), **22**, 129 (1961).

respectively, formed in the reaction of 4-methylcyclohexene with peracid.[26] As a control, a known mixture of the two isomeric ketones was subjected to the oxidizing solution for a comparable period of time; the recovered mixtures had the same composition as the starting material.

Epoxides of 3-Methylcyclohexene.—Mixed hydride reduction of this epoxide mixtures gave all four possible alcohol products; *cis*-2- (53%), *cis*-3- (4%), *trans*-3- (28%), and *trans*-2-methylcyclohexanol (15%). Lithium aluminum hydride alone gave comparable results. In view of the failure of the mixed reagent to give cleanly axial products, it is not possible to assign unequivocably the precursor epoxide of each alcohol.[30] However, the preponderance of *cis* alcohols suggests strongly that *cis* epoxide is the major product of the peracid reaction.

Kinetic Procedure.—Rates were determined by following loss of peracid iodometrically. Aliquots of ethereal solution were removed periodically from tightly stoppered flasks held in a constant temperature bath at 25.0°. Good second-order plots were obtained through at least 80% of reaction.

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[30] Assuming only diaxial opening with the mixed reagent, the present data suggest that axial alkyl conformations are contributing appreciably to the reduction transition states.

The Simmons–Smith Reaction of *trans,trans,cis*-1,5,9-Cyclododecatriene

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The title reaction was carried out with varying mole ratios of methylene iodide to obtain mono- (II), bis- (III and IV), and triscyclopropane derivatives (V). The Simmons–Smith reagent attacks preferentially one of the *trans* olefinic bonds of the triene I and then the *cis* double bond of the diene II. Reductive cleavage of the cyclopropane ring of these products (II and V) under various conditions failed to afford the corresponding ring-enlargement products.

As a step in attempted ring-enlargement of *trans,trans,cis*-1,5,9-cyclododecatriene (I)[1] the Simmons–Smith reaction[2] of this triene has been examined and the results, as summarized in Table I, are discussed in the present paper.

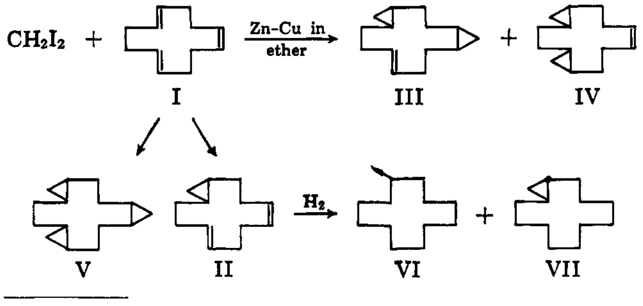
TABLE I

MOLE RATIOS OF REAGENTS AND COMPOSITION OF PRODUCTS

Methylene iodide to I, mole ratio	% yield[a]		
	II[b]	III and IV[c]	V
1	58	8	Trace
2	25	30	7
10	0	0	54[d]

[a] The yields were calculated based on the weight of isolated mixture and peak areas in the analytical gas chromatogram. [b] The fraction contains less than 5% of an isomer. See the text. [c] This is a mixture of III and IV in 4:1 mole ratio, respectively. [d] A single peak.

The methylenation was carried out in the standard way[2] with varying mole ratios of methylene iodide to I and the products were subjected to analytical gas chromatography. Each component was isolated by preparative gas chromatography and information concerning the sites of attack during methylenation was obtained by examination of the infrared spectra.



The monocyclopropane fraction (II) was practically homogeneous upon gas chromatography, although a small shoulder (less than 5% in its area) appeared at the high retention time side of the peak. The infrared spectrum showed both the *trans* and *cis* double bond absorptions at 960 and 700 cm.$^{-1}$, respectively. Therefore, II is formed by the attack of one of the *trans* bonds of the triene I. The minor component would probably have arisen from the attack of the *cis* bond of I, but attempted isolation of this isomer failed. Hydrogenation of II with 10% palladium-on-charcoal catalyst gave a mixture of methylcyclododecane (VI) and *trans*-bicyclo[10.1.0]tridecane (VII), VII being converted into VI by exhaustive hydrogenation. The *trans*-bicyclotridecane (VII) thus obtained was clearly distinguished from the authentic *cis* isomer which was prepared by the Simmons–Smith reaction of *cis*-cyclododecene.[3] The differentiation was made on the basis of the retention times in gas chromatography and comparison of the infrared spectra.

With 2 moles of the Simmons–Smith reagent a mixture of biscyclopropane derivatives III and IV was obtained as a major fraction, which gave two peaks in the ratio of 4:1 upon gas chromatography. Methylenation of the pure monoadduct (II) also gave a product which showed an identical gas chromatogram. The substance giving the predominant peak (III) was preparatively isolated and its infrared spectrum was examined. No *cis* absorption was detected in the neighborhood of 700 cm.$^{-1}$, while the *trans* absorption at 960 cm.$^{-1}$ and the cyclopropane absorption at 1020 cm.$^{-1}$ were clearly recognized. The substance giving the minor peak could not be isolated pure, but the presence of *cis* absorption at 700 cm.$^{-1}$ in the crude biscyclopropane fraction indicated that this was very probably the isomer IV. Accordingly, the further attack of II by the Simmons–Smith reagent takes place at the *cis* bond rather than at the *trans* bond. The selectivity (4:1), however, is not so sharp as the attack of the original triene I.

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[1] G. Wilke, *Angew. Chem.*, **75**, 10 (1963).

[2] (a) E. P. Blanchard and H. E. Simmons, *J. Am. Chem. Soc.*, **86**, 1337 (1964); (b) H. E. Simmons, E. P. Blanchard, and R. D. Smith, *ibid.*, **86**, 1347 (1964).

[3] For the preparation of cyclododecene, see H. Nozaki and R. Noyori, *J. Org. Chem.*, **30**, 1652 (1965).